

We claim:

1. A neutralizing bispecific fusion protein capable of binding to two sites on a target protein, comprising a first binding domain capable of binding to an inducing site on the target protein, thereby exposing an induced epitope; a second binding domain capable of forming a neutralizing complex with an induced epitope of the target protein; and a linker connecting the first domain to the second domain, wherein at least one of the first and second binding domains comprises a binding portion of a variable region of an antibody heavy or light chain.
2. A protein according to claim 1, wherein the first binding domain comprises a binding portion of a variable region of an antibody heavy or light chain.
3. A protein according to claim 2, wherein the first binding domain comprises an epitope binding domain of an antibody.
4. A protein according to claim 3, wherein the first domain comprises a single-chain Fv (SCFv).
5. A protein according to claim 3, wherein the antibody binding domain mimics a biological activity of a CD4 molecule in binding to the inducing site and exposing the inducing epitope.
6. A protein according to claim 5, wherein the antibody binding domain is derived from a CD4 anti-idiotypic antibody.
7. A protein according to claim 1, wherein the target protein is a viral envelope protein of a virus.
8. A protein according to claim 7, wherein the virus is human immunodeficiency virus (HIV).
9. A protein according to claim 8, wherein the viral envelope protein is gp120.
10. A protein according to claim 2, wherein the first binding domain is derived from a CD4 molecule.
11. A protein according to claim 10, wherein the first binding domain comprises CD4 D1 or CD4D1D2.
12. A protein according to claim 11, wherein the first binding domain is sCD4.
13. A protein according to claim 1, wherein the second binding domain comprises a binding portion of a variable region of an antibody heavy or light chain.
14. A protein according to claim 13, wherein the second binding domain comprises a binding domain of an antibody.
15. A protein according to claim 14, wherein the second binding domain comprises a single-chain Fv (SCFv).
16. A protein according to claim 15, wherein the SCFv is selected from the group consisting of SCFv17b, SCFv48d and SCFvCG10.
17. A protein according to claim 14, wherein the antibody binding domain is derived from a neutralizing monoclonal antibody.

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18. A protein according to claim 17, wherein the neutralizing monoclonal antibody is selected from the group consisting of 17b, 48d, and CG10.
19. A protein according to claim 9, wherein the second binding domain mimics a biological activity of an HIV coreceptor molecule in binding to gp120.
20. A protein according to claim 19, wherein the second binding domain comprises a peptide fragment of an HIV coreceptor.
21. A protein according to claim 20, wherein the HIV coreceptor is a chemokine receptor.
22. A protein according to claim 21, wherein the chemokine receptor is selected from the group consisting of CXCR4, CCR2B, CCR3, and CCR5, CCR8, CCR9, CX3CR1, US28, or the chemokine receptor related proteins including STRL33, GPR15, APJ, ChemR23, and BLTR.
23. A protein according to claim 9, wherein the induced epitope comprises at least one coreceptor binding determinant of gp120.
24. A protein according to claim 9, wherein the inducing site is a gp120 CD4 binding site.
25. A protein according to claim 14, wherein the binding domain of the antibody is capable of binding to at least one coreceptor binding determinant of gp120.
26. A protein according to claim 1, wherein the linker maintains the second binding domain in binding proximity to the induced epitope when the first binding domain is bound to the inducing site.
27. A protein according to claim 26, wherein the linker is substantially flexible.
28. A protein according to claim 26, wherein the linker is 15-100 angstroms (Å) long.
29. A protein according to claim 26, wherein the linker is 10-100 amino acid residues in length.
30. A protein according to claim 26, wherein the linker comprises at least one occurrence of an amino acid sequence as represented by SEQ ID NO: 1.
31. A protein according to claim 1, wherein the linker comprises at least one occurrence of an amino acid sequence represented by SEQ ID NO: 1.
32. A protein according to claim 31, wherein the linker comprises an amino acid sequence represented by SEQ ID NO: 2.
33. A functional recombinant bispecific fusion protein capable of binding to two sites on gp120, comprising:
 - a) sCD4;
 - b) SCFv(17b); and
 - c) a linker of a length sufficient to maintain the SCFv(17b) in binding proximity an SCFv(17b) epitope when sCD4 is bound to gp120.
34. A protein according to claim 33, wherein the linker has an amino acid sequence as represented by SEQ ID NO: 2
35. An isolated nucleic acid molecule encoding a protein according to claim 34.

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36. A nucleic acid molecule according to claim 35, wherein the nucleic acid sequence is represented by SEQ ID NO: 3.

37. A protein encoded for by the nucleic acid molecule according to claim 36.

38. An isolated nucleic acid molecule encoding a protein according to claim 1.

39. The nucleic acid molecule according to claim 38, having nucleic acid sequence SEQ ID NO: 4.

40. A transgenic eukaryotic cell comprising the isolated nucleic acid molecule according to claim 38.

41. A method for producing in a eukaryotic cell a functional recombinant bispecific fusion protein capable of binding two sites on a target protein, comprising the steps of:

- a) transfecting the eukaryotic cell with a recombinant nucleic acid molecule according to claim 38;
- b) culturing the transfected eukaryotic cell under conditions that cause production of the protein; and
- c) recovering the protein produced by the cultured eukaryotic cell.

42. The method of claim 41, wherein the eukaryotic cell is a mammalian cell.

43. The method of claim 41, wherein recovering the protein comprises:

- a) identifying the protein by the presence of a molecular tag; and
- b) separating the protein having the molecular tag so identified from molecules without the tag, so as to recover the protein produced by the cultured eukaryotic cell.

44. A method for inactivating a gp120 protein, comprising the step of: contacting the gp120 protein with a protein according to claim 9, or a variant protein, analog or mimetic thereof.

45. A method for neutralizing a human immunodeficiency virus, comprising the step of: contacting the human immunodeficiency virus with a protein according to claim 9, or a variant protein, analog or mimetic thereof.

46. A method for blocking and preventing the binding of a viral or recombinant gp120 protein to soluble CD4 or lymphocyte CD4, comprising the step of:

contacting the gp120 protein with a protein according to claim 9, or a variant protein, analog or mimetic thereof.

47. A method for inhibiting HIV virus replication or infectivity in a subject, comprising administering to the subject an amount of the protein according to claim 9, or a variant protein, analog or mimetic thereof, sufficient to inhibit HIV virus replication or infectivity.

48. A composition comprising the protein according to claim 1, or a variant protein, analog or mimetic thereof.

49. A pharmaceutical composition comprising the protein according to claim 1, or a variant protein, analog or mimetic thereof, and a pharmaceutically acceptable carrier.

- 1 50. The method according to claim 47, wherein the protein is administered in the form of a pharmaceutical composition.
51. A protein analog, derivative, or mimetic of the protein of claim 1.
52. A kit for treatment and/or prevention of HIV infection, comprising a clinically effective dose of the neutralizing bispecific fusion protein of claim 1.
53. The kit of claim 52, further comprising instructions.
54. The kit of claim 53, wherein the instructions include directions for administering at least one dose of the neutralizing bispecific fusion protein to a subject in need of such treatment.
55. The kit of claim 52, wherein the neutralizing bispecific fusion protein is provided in the form of a pharmaceutical composition.

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